Use of Contemporary Imaging Techniques for Electrophysiological and Device Implantation Procedures

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iREVIEW

STATE-OF-THE-ART REVIEW

Use of Contemporary Imaging Techniques for Electrophysiological and Device Implantation Procedures

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JACC: CARDIOVASCULAR IMAGING CME/MOC/ECME

CME/MOC/ECME Editor: Ragavendra R. Baliga, MD

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CME/MOC/ECME Objective for This Article: After reading this article the reader should be able to discuss how cardiac imaging can be helpful in: 1) prediction of arrhythmic risk of sudden cardiac death in patients with heart disease; 2) catheter ablation of atrial fibrillation or ventricular tachycardia; 3) cardiac resynchronization therapy; 4) increasing effectiveness of cardiac electrophysiological procedures; and 5) delivering patient-specific therapies in ablation and cardiac implantable electronic devices.

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ABSTRACT

Recent technological advances in cardiac imaging allow the visualization of anatomic details up to millimeter size in 3-dimensional format. Thus, it is not surprising that electrophysiologists increasingly rely upon cardiac imaging for the diagnosis, treatment, and subsequent management of patients affected by various arrhythmic disorders. Cardiac imaging methods reviewed in the present work involve: 1) the prediction of arrhythmic risk for sudden cardiac death in patients with heart disease; 2) catheter ablation of atrial fibrillation or ventricular tachycardia; and 3) cardiac resynchronization therapy. Future integration of diagnostic and interventional cardiac imaging will further increase the effectiveness of cardiac electrophysiological procedures and will help in delivering patient-specific therapies with ablation and cardiac implantable electronic devices. (J Am Coll Cardiol Img 2020;13:851–65)

Over the past 2 decades, impressive technological advances in cardiac imaging have occurred that allow the visualization of anatomic details up to millimeter size in 3-dimensional (3D) format and assessment of myocardial deformation with unprecedented time resolution. Thus, it is not surprising that electrophysiologists have increasingly relied upon cardiac imaging for the diagnosis, treatment, and subsequent management of patients affected by various arrhythmic disorders. In this review (**Central Illustration**), we consider selected arrhythmic disorders for which contemporary cardiac imaging technology is integral to diagnostic and follow-up workflow: 1) prediction of arrhythmic risk for sudden cardiac death in selected patient populations; 2) catheter ablation of arrhythmias; and 3) cardiac resynchronization therapy (CRT).

CARDIOVASCULAR IMAGING IN THE PREDICTION OF ARRHYTHMIC RISK FOR SUDDEN CARDIAC DEATH IN SELECTED PATIENT POPULATIONS

Risk assessment of ventricular arrhythmias is of paramount importance in patients with heart disease. Although a recent meta-analysis documented that the rate of sudden cardiac death declined substantially among ambulatory patients with heart failure (HF) and reduced left ventricular ejection fraction (LVEF) (1), sudden cardiac death still represents a major cause of cardiovascular death. Current guidelines for the use of implantable cardioverter-defibrillators (ICDs) in primary prevention are based mostly on LVEF values (2,3), despite the fact that this parameter is considered an unsatisfactory risk marker for sudden cardiac death. Indeed, a severely depressed LVEF is a low-specificity marker in differentiating risk for sudden cardiac death from risk for death associated with comorbidities or with the evolution of HF. Similarly, sudden cardiac death can occur in patients with normal or mildly depressed LVEFs. Therefore, abnormal myocardial structure (substrate) rather than volumetric and functional assessment is becoming the new reference for the evaluation of sudden cardiac death risk. Although sudden cardiac death in patients with prior myocardial infarction is attributed mainly to the result of re-entrant ventricular arrhythmias originating from surviving myocardial strain embedded into infarcted myocardium (**Figure 1**), the mechanism in nonischemic cardiomyopathy is less well understood but possibly related to fibrosis. Although multiple imaging modalities can be used to ascertain myocardial scar and fibrosis, cardiac magnetic resonance (CMR) late gadolinium enhancement (LGE) holds the greatest promise for noninvasive risk assessment of ventricular arrhythmias. LGE by CMR has recently become a widely available clinical diagnostic procedure to visualize in vivo myocardial scar and fibrosis in patients with a variety of myocardial diseases and has emerged as the gold standard for identifying myocardial fibrosis. Furthermore, the recent addition of high-resolution

LGE imaging to the CMR protocol has significantly improved the performance of CMR in detecting small left ventricular (LV) or right ventricular substrates, particularly in patients without structural heart disease as diagnosed on transthoracic echocardiography or coronary angiography (4).

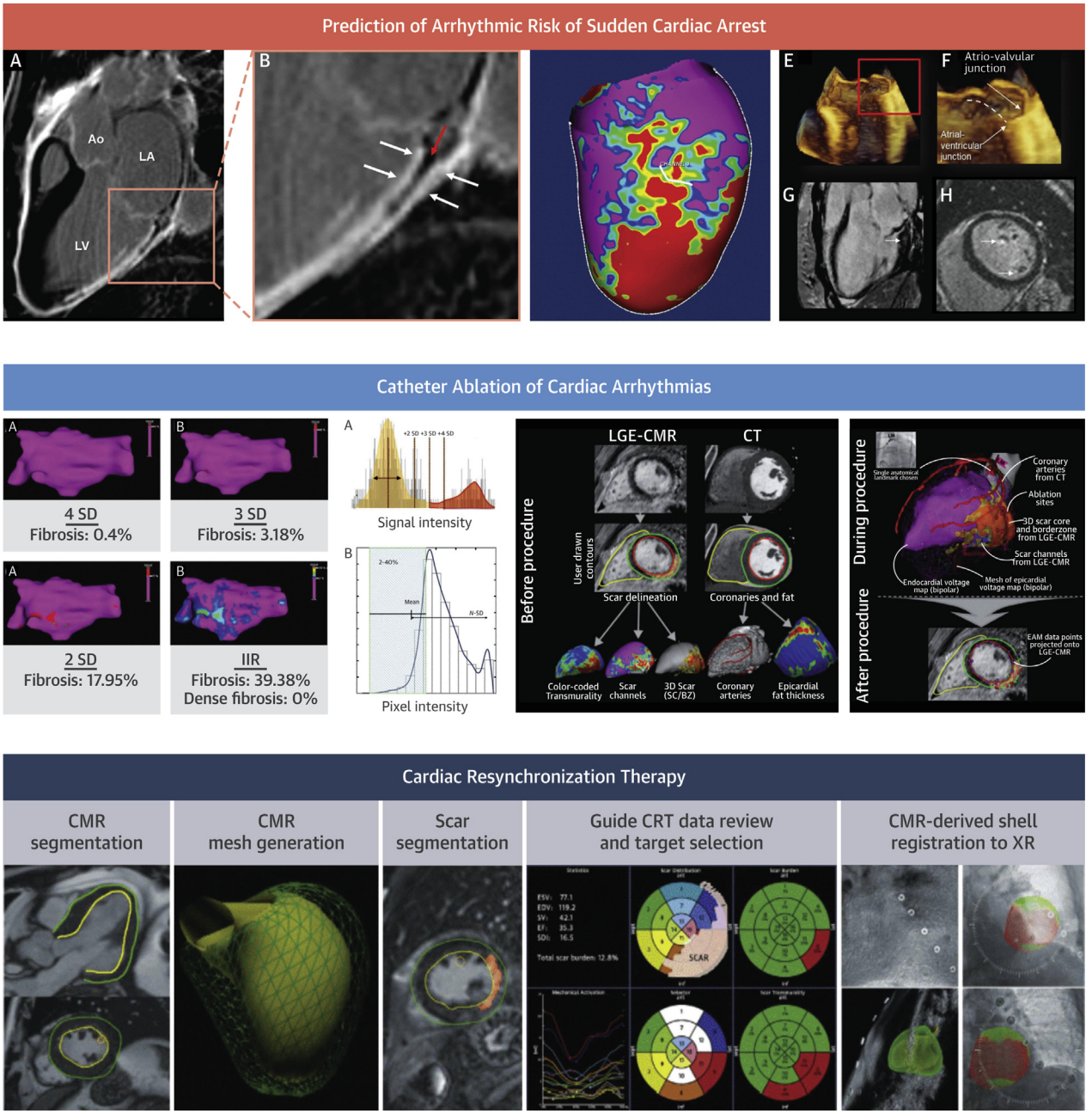
RISK ASSESSMENT IN PATIENTS WITH ISCHEMIC AND NONISCHEMIC CARDIOMYOPATHY BY CMR. In a recent meta-analysis, Disertori et al. (3) evaluated the predictive value of LGE for ventricular tachyarrhythmia in patients with ischemic and nonischemic cardiomyopathy with ventricular dysfunction, including 2,850 patients collected from 19 different studies with a mean follow-up time of 2.8 years. The investigators demonstrated that LGE represents a powerful predictor of ventricular tachyarrhythmia events in patients with ventricular dysfunction of ischemic and nonischemic etiology (**Figures 1 and 2**). The composite arrhythmic endpoint was reached in 23.9% of patients with positive results on LGE testing (annualized event rate 8.6%) compared with 4.9% of patients with negative results (annualized event rate 1.7%) ($p < 0.0001$). LGE correlated with arrhythmic events in the different patient groups. In the overall population, the pooled odds ratio was 5.62 (95% confidence interval [CI]: 4.20 to 7.51), with no significant differences between ischemic and nonischemic patients. In a subgroup of 11 studies ($n = 1,178$) with mean LVEF ≤30%, the pooled odds ratio for the arrhythmic events increased to 9.56 (95% CI: 5.63 to 16.23), with a negative likelihood ratio of 0.13 (95% CI: 0.06 to 0.30). Notably, the odds ratio was almost doubled in studies with mean LVEFs ≤30% compared with >30%, thus indicating that the prognostic power of LGE for ventricular arrhythmias is particularly strong in patients with severely depressed LVEFs. In addition, it indicates that even in a challenging group of patients such as those with LVEFs >30%, LGE can be used as a reliable marker for predicting arrhythmic events. The importance of evaluating LGE in patients with nonischemic cardiomyopathy has become relevant following the recent findings of DANISH (Danish Study to Assess the Efficacy of ICDs in Patients With Non-Ischemic Systolic Heart Failure on Mortality) (5), which showed no reduction in overall mortality among patients with nonischemic cardiomyopathy with high rates of guideline-recommended pharmacological therapy. More recently, Leyva et al. (6) studied nonischemic cardiomyopathy CRT patients with midwall fibrosis ($n = 68$) compared with those without midwall fibrosis ($n = 184$). They showed that CRT with a defibrillator was superior to CRT only in patients with midwall fibrosis (**Figure 2**); however, a large prospectively designed controlled trial is needed to confirm these findings.

Advanced LGE post-processing techniques have been recently developed to better quantify myocardial scar tissue and to differentiate between scar core and border zone. The border zone extension and scar heterogeneity have been associated with inducibility of ventricular tachyarrhythmias and mortality prediction in patients with structural heart disease. This hypothesis was recently tested in the GAUDI-CRT (Life-Threatening Arrhythmic Events and Sudden Cardiac Death in Cardiac Resynchronization Therapy Patients) trial, which included 217 CRT patients (7). Pre-procedural LGE was obtained and analyzed to identify scar presence or absence, to quantify the amount of core and border zone, and to depict border zone distribution. During a median follow-up period of 35.5 months, appropriate ICD therapy or sudden cardiac death occurred in 25 patients (11.5%) and did not occur in CRT patients without myocardial scar. Among patients with scar ($n = 125$ [57.6%]), those with ICD therapies or sudden cardiac death exhibited greater scar mass (38.7 ± 34.2 g vs. 17.9 ± 17.2 g; $p < 0.001$), scar heterogeneity (border zone mass/scar mass ratio 49.5 ± 13.0 vs. 40.1 ± 21.7; $p = 0.044$), and border zone channel mass (3.6 ± 3 g vs. 1.8 ± 3.4 g; $p = 0.018$). Border zone mass and channel mass were the strongest predictors of arrhythmic events. An automated algorithm based on scar mass and absence of border zone channels identified 68.2% ($n = 148$) without ICD therapy or sudden cardiac death during follow-up with 100% negative predictive value (**Figure 3**, Video 1). Although the findings of this study require confirmation in larger and properly designed clinical trials, especially for the ICD population, they are extremely promising, as they indicate the possibility to accurately stratify risk in patients with HF on the basis of morphological and anatomic characteristics. Interestingly, Haugaa et al. (8) hypothesized that in patients after myocardial infarction, mechanical dispersion, as assessed by longitudinal strain speckle-tracking echocardiography, may be correlated with scar heterogeneity and therefore with risk for arrhythmias. In each patient, the investigators defined mechanical dispersion as the SD of 16 different time intervals to maximum myocardial deformation. They found that mechanical dispersion was greater in ICD patients with recorded ventricular arrhythmias compared with those without (85 ±

ABBREVIATIONS AND ACRONYMS

3D = 3-dimensional
AF = atrial fibrillation
CI = confidence interval
CRT = cardiac resynchronization therapy
CMR = cardiac magnetic resonance
HF = heart failure
ICD = implantable cardioverter-defibrillator
LA = left atrial
LV = left ventricular
LVEF = left ventricular ejection fraction
LGE = late gadolinium enhancement
MVP = mitral valve prolapse
PVI = pulmonary vein isolation
VT = ventricular tachycardia

CENTRAL ILLUSTRATION **Use of Contemporary Imaging Techniques for Electrophysiological and Device Implantation Procedures**



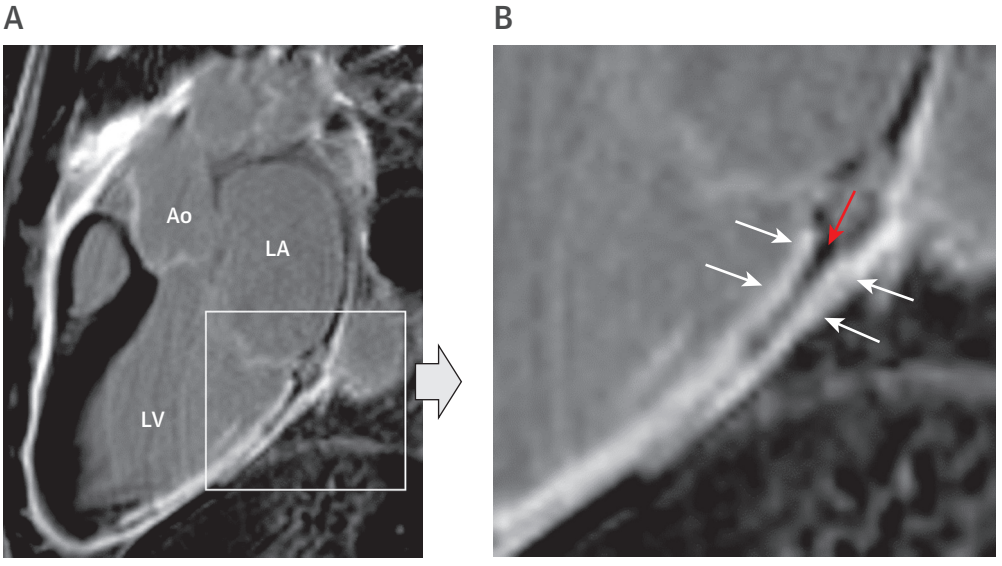
Auricchio, A. et al. J Am Coll Cardiol Img. 2020;13(3):851-65.

See Figures 1 to 3 and 6 to 8 for details.

29 ms vs. 56 ± 13 ms; $p < 0.001$). By Cox regression, mechanical dispersion was a strong and independent predictor of arrhythmias requiring ICD therapy (hazard ratio: 1.25 per 10-ms increase; 95% CI: 1.1 to 1.4; $p < 0.001$) (8).

RISK ASSESSMENT IN PATIENTS WITH MITRAL VALVE PROLAPSE. Degenerative mitral valve prolapse (MVP) is the most frequent cause of primary mitral regurgitation in Western countries, affecting 1% to 3% of the general population (9). A small but notable

FIGURE 1 Late Gadolinium Enhancement in a Previous Inferior-Posterior Myocardial Infarction



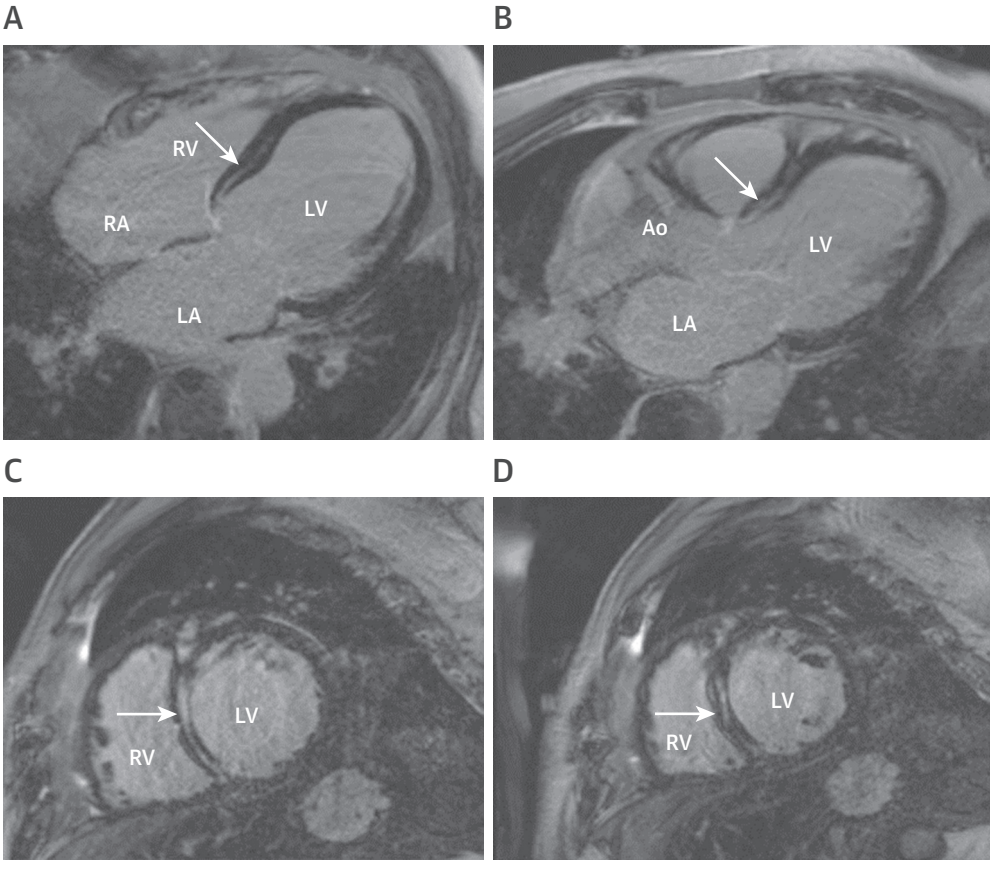
(A) Long-axis view showing an extensive scar on the posterior wall **(white area)** as a result of a previous inferior-posterior myocardial infarction. **(B)** Magnified image of the apical portion of the posterior wall **(white square in A)**, presenting the border zone of inferior-posterior myocardial infarction and 2 layers of normal myocardium **(white arrows)** surrounding 1 layer of scar **(red arrow)**. This particular substrate may trigger ventricular tachyarrhythmias. Ao = aorta; LA = left atrium; LV = left ventricle.

proportion of patients with MVP may develop malignant arrhythmias and sudden cardiac death (10); the estimated rate of sudden cardiac death attributed to ventricular fibrillation in patients with primary MVP remains exceedingly low (0.2% to 0.4% per year) (11). Several morphological aspects, such as bileaflet MVP with diffuse leaflet redundancy and thickening (due to accumulation of proteoglycans through the spongiosa), chordae elongation, and annular dilation, electrocardiographic abnormalities, severity of mitral valve regurgitation, and LV dysfunction have been associated with arrhythmias in MVP (12). An anatomic substrate for promoting electric instability was described by Sanfilippo et al. (13) and subsequently by Han et al. (14). These investigators demonstrated the presence of LGE on valve leaflets (indicating the expansion of spongiosa due to proteoglycans accumulations) and on the tips of papillary muscles (indicating fibrosis). Interestingly, the presence of fibrosis at the papillary muscles tip was more often observed in a subgroup of patients with arrhythmic MVP. More recently, Basso et al. (15) confirmed and extended these observations. In 43 young patients (age range 10 to 40 years) with MVP and myxomatous valve who died of sudden cardiac death, the investigators found patches of replacement-type fibrosis on papillary muscles and on subendocardial-midmural layers of basal posterior wall, just below the posterior valve leaflet (**Figure 4**, Videos 2 and 3). They hypothesized that systolic mechanical stretch of myocardium closed to the mitral valve might have accounted for injuries, eventually leading to replacement-type fibrosis. Marra et al. (16) provided further evidence for this hypothesis, finding that mitral annular disjunction, defined as a separation between the left atrial (LA) wall-mitral hinge line and the LV free wall, is a constant feature in patients with arrhythmic MVP (**Figure 4**). They hypothesized that this peculiar morphological aspect might contribute to the systolic stretch of the myocardium close to the valve and, as a result, to the propensity to develop regional LV fibrosis and electric instability. According to their conclusions, the genesis of malignant arrhythmias in MVP may be recognized in the deadly combination of a substrate (papillary muscle tips and basal free wall myocardial fibrosis) and a trigger (i.e., myocardial stretch exacerbated by mitral annular dysfunction) (**Figure 5**).

CARDIOVASCULAR IMAGING IN CATHETER ABLATION OF ARRHYTHMIAS

ATRIAL FIBRILLATION. The link between atrial fibrosis and atrial fibrillation (AF) onset and progression is well known, and the possibility to visualize

FIGURE 2 Midwall Fibrosis Evaluation

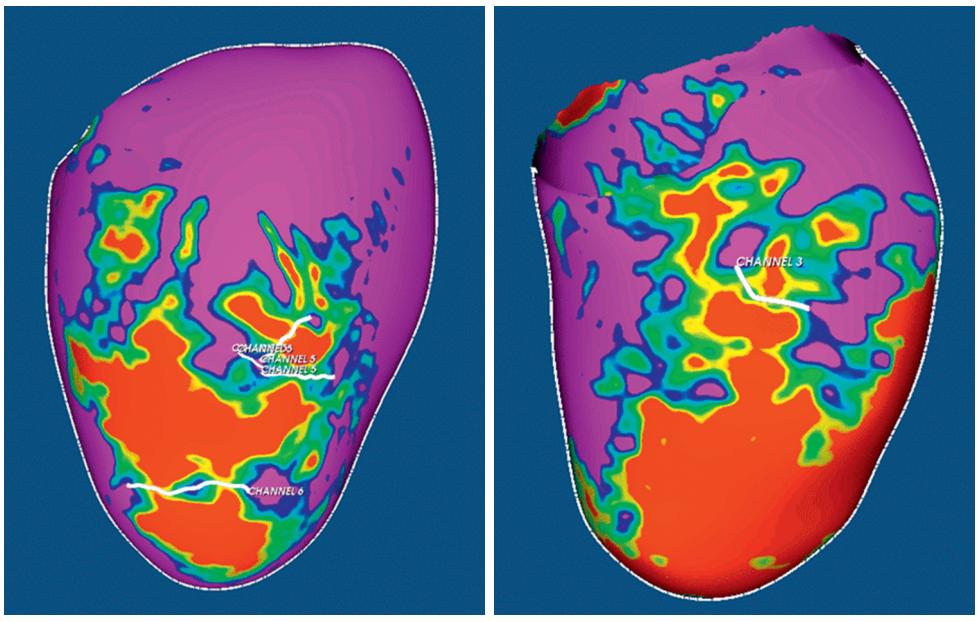


Midwall fibrosis as detected with late gadolinium enhancement in a patient with nonischemic cardiomyopathy in **(A)** 4-chamber, **(B)** long-axis, and **(C,D)** short-axis views. AO = aorta; LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ventricle.

atrial fibrosis by CMR has presented unprecedented diagnostic and interventional opportunities. Consequently, pre-procedural assessment of atrial fibrosis to screen out patients undergoing pulmonary vein ablation may significantly help in improving the cost/benefit and risk/effectiveness ratios of catheter ablation in patients with AF. Likewise, visualization of fibrosis area and integration into 3D mapping systems to guide AF catheter ablation strategy (e.g., pulmonary vein isolation [PVI] or additional lines) may improve outcomes in patients undergoing catheter ablation. LGE on CMR can detect ablated regions, together with the evolution of their pattern and signal intensity over time, likely suggesting initial edema followed by scar formation; this possibility may further help in the management of those patients presenting with AF recurrence. Finally, visualization of fibrosis and inclusion in computer modeling is the next frontier in cardiac electrophysiology to develop patient-specific ablation strategy.

The DECAAF study by Marrouche et al. (17) was the first multicenter, prospective, observational cohort study of patients diagnosed with paroxysmal and persistent AF undergoing their first catheter ablation with PVI. CMR imaging was performed before ablation, and atrial fibrosis was quantified and classified into stages: 1 (<10% of the atrial wall); 2 (≥10% to <20%); 3 (≥20% to <30%); and 4 (≥30%). The cumulative incidence of recurrent arrhythmia at 1 year for stages 1, 2, 3, and 4 was 15.3%, 32.6%, 45.9%, and 51.1%, respectively. This and several subsequent studies emphasize the importance of baseline imaging and quantification of atrial scar as a key predictor of procedural outcomes after PVI. Altogether, these studies are precursors to further investigations of substrate modification in addition to PVI, specifically

FIGURE 3 **Three-Dimensional Color-Coded Signal Intensity Maps**

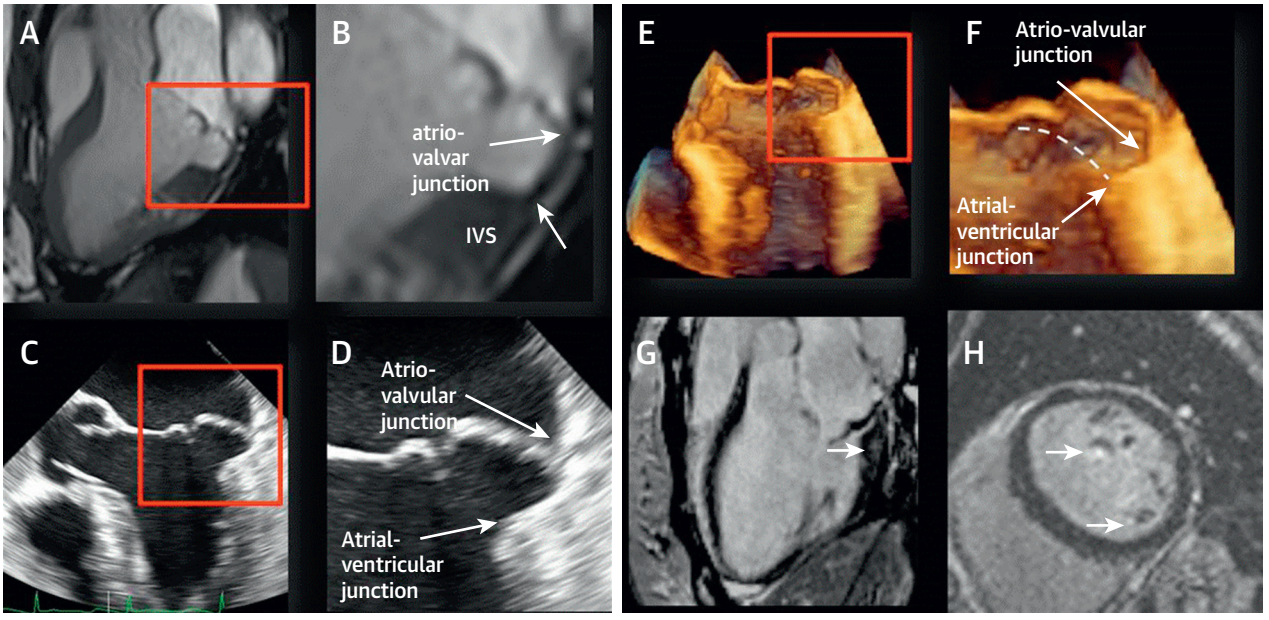


The signal intensity maps in 5 transmural shells were obtained with specific cardiac magnetic resonance sequences representing the scar, shape, and distribution of the scar tissue across the wall thickness. **Purple** represents normal tissue, **green** the border zone, and **red** scar tissue. Channels, possible ablation targets, are indicated as well (see also Video 1).

in patients with severe atrial scarring as detected by CMR. Recent observations regarding the use of CMR for fibrosis imaging are, however, conflicting. A prospective single-center experience of 149 consecutive patients (64 persistent, 85 paroxysmal) undergoing AF ablation showed that delayed enhancement detected by CMR within the LA walls using standard clinical scanners and typical pulse sequence parameters was uncommon (n = 5, prevalence 3%) and, when present, did not correlate with AF type or risk for AF recurrence (18). These results clearly conflict with other investigational data (19). As suggested by Pontecorboli et al. (20) in a recent review, it is clear that fibrosis and scar detection by CMR is not without pitfalls. Indeed, the development of standardized specific protocols and uniform cutoffs for fibrosis detection may lead to improved accuracy and reproducibility (**Figure 6**). Furthermore, relative atrial wall thickness (which is similar to the spatial resolution of CMR) represents a significant anatomic challenge in the 3D volumetric estimation of fibrosis and scar by this imaging technique. This becomes highly relevant when considering the experimental evidence that in the early stage of the disease, the fibrosis is mostly confined to the epicardial layers and progressively expands transmurally. Finally, although most of the studies have focused on fibrosis and scar assessment in the left atrium, structural changes have remained nearly unexplored in the right atrium, a cardiac chamber that is now becoming an ablation target in non-PVI-dependent AF. Outcomes among patients with persistent AF after PVI are still a matter of considerable debate. Although some may benefit from ablation, in others, sinus rhythm cannot be maintained for a reasonable amount of time despite extensive ablation (21). Parwani et al. (22) found that LA strain is lower in patients with recurrence of atrial arrhythmias after PVI (n = 55) than those without recurrence (LA strain 9.7 ± 2.4% vs. 16.2 ± 3.0%; $p < 0.001$), concluding that low (<10%) LA strain predicts recurrence of AF (hazard ratio: 6.4; 95% CI: 2.4 to 16.9; $p < 0.001$). This finding strongly suggests a profound link between electric and mechanical function, a research area that has not received sufficient attention.

VENTRICULAR TACHYCARDIA. Over the past 2 decades, the role of cardiac imaging in patients with ventricular tachycardia (VT) has progressed from making relatively crude measurements of LVEF to defining intricate details of scar architecture and, perhaps most important, providing complementary

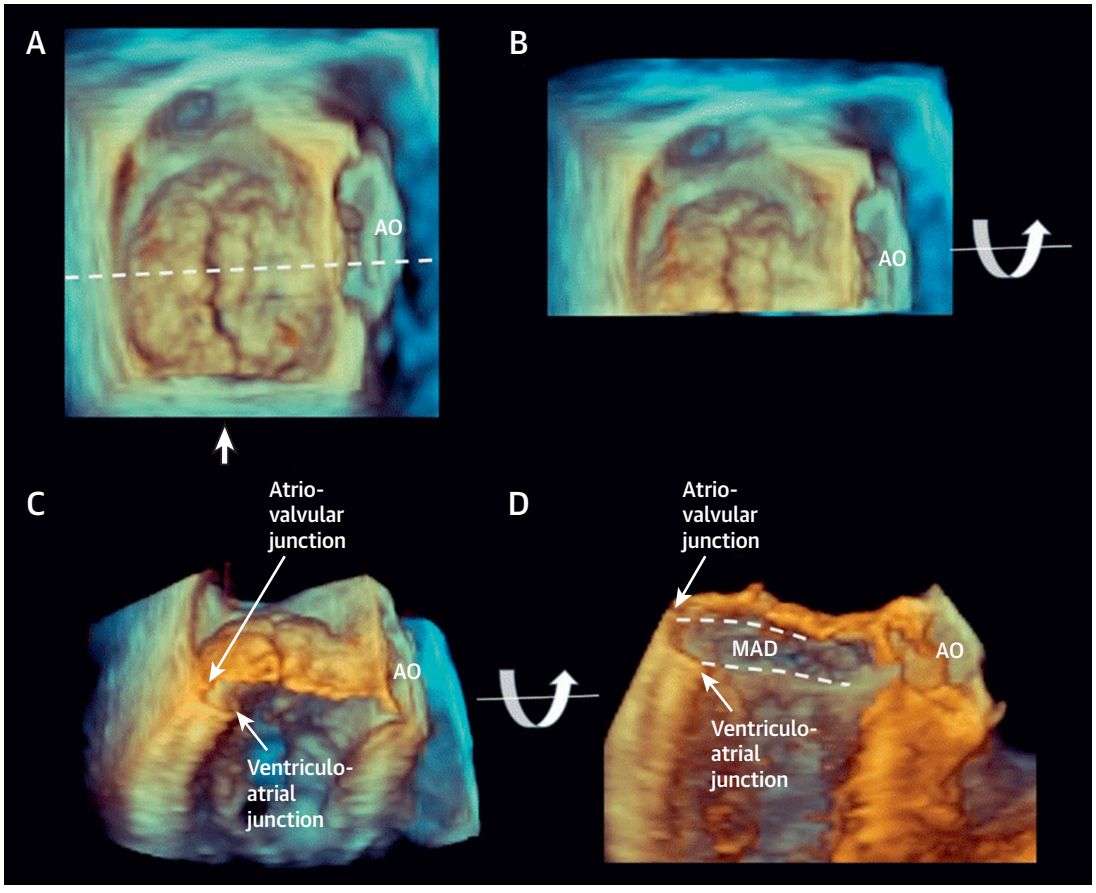
FIGURE 4 Cine Cardiac Magnetic Resonance Showing a Mitral Valve Disjunction in a Patient With Mitral Valve Prolapse



The **area in the red box** is magnified in **B**. The image clearly shows that the hinge of the posterior mitral leaflet is attached to the atrial wall. forming the atriovalvular junction, while the crest of interventricular septum (IVS) is far from the mitral hinge line. **(C)** Two-dimensional and **(E)** 3-dimensional transesophageal echocardiography showing the same patient as in **(A)**. The **areas in the red boxes** are magnified in **D and F**, respectively. This peculiar morphology is thought to contribute to the systolic stretch of the basal posterior myocardial wall and tips of papillary muscles developing regional left ventricular fibrosis **(arrows)** and electric instability (see Videos 2 and 3).

information on electric activation. This latter approach was extensively covered in a recent review by Mahida et al. (23). Electrophysiological substrate mapping during sinus or paced rhythm allows the characterization of scar areas to identify so-called conducting channels, the electrophysiological basis for re-entry circuits of VT. These channels can be identified by intracardiac voltage mapping or electrogram analysis and are considered the ablation target. Radiofrequency applications at the conducting channels entrance (the so-called scar dechanneling technique) can homogenize the scar without extensive ablation and could possibly increase the ablation efficiency (**Figures 3 and 7**). High-resolution contrast-enhanced CMR accurately delineates the scar and makes it possible to differentiate between scar core and border zone and, together with advanced post-processing, to allow the visualization of the border areas inside the scar as corridors of viable tissue connecting the healthy myocardium (24). These corridors correlate with the conducting channels on electroanatomic mapping. CMR-based visualization of scar characteristics is helpful in VT ablation procedures (**Figures 3 and 7**) (25). As recently reported by Andreu et al. (26), the ablation strategy of scar dechanneling alone results in lower recurrence and mortality rates in more than one-half of patients, despite the required limited ablation extent compared with a more traditional ablation approach. The investigators compared the outcomes of 54 patients (34%) who had pixel signal intensity maps were obtained from a high-resolution 3-T LGE CMR study and imported into the navigation system to aid in VT substrate ablation, with those of the remaining 105 patients, who had pixel signal intensity maps could either be obtained or be imported into the navigation system. The use of pixel signal intensity maps to guide the ablation minimized the number of radiofrequency applications and ablation delivery time needed. This was also associated with a higher rate of immediate success after substrate ablation, thus suggesting better identification of the arrhythmogenic substrate and target ablation site. Notably, the information obtained from CMR, showing the wall distribution of the scar, contributed to the decision on the optimal approach (endocardial, epicardial, or combined), which could explain the reported better outcomes in the CMR-aided group compared with the

FIGURE 5 3-Dimensional Transesophageal Echocardiographic View From Overhead Showing a Patient With Barlow Disease



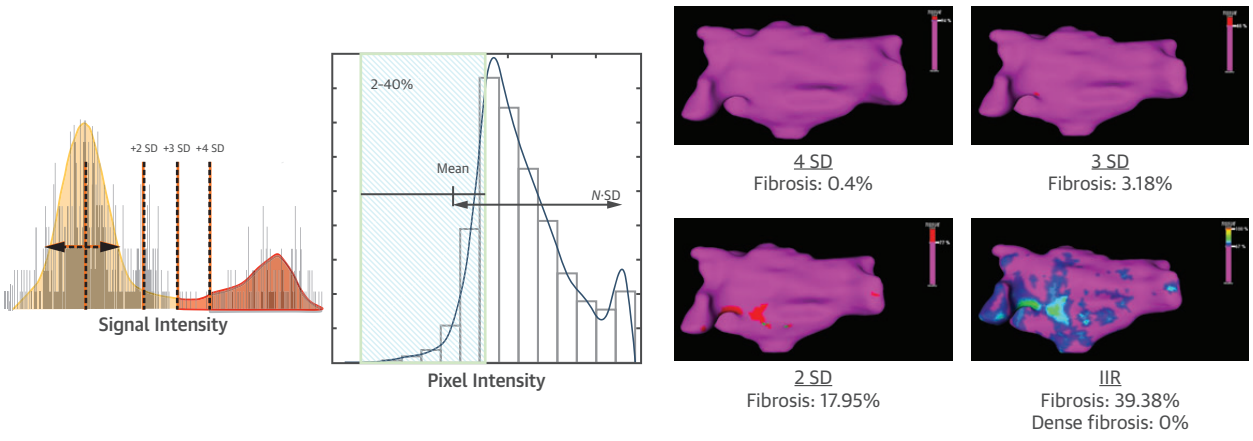
From this perspective, the mitral-aortic disjunction (MAD) is not visible. A **crop in the direction of the thick arrow** up to the center of the valve **(dotted line) (A)** leads to half valve **(B)**. A progressive rotation **(curved arrow)** around the x-axis **(C,D)** reveals the MAD as the rectangular space between the atriovalvular junction and the ventricular-atrial junction. AO = aorta.

other patients. However, pixel signal intensity alone was not sufficient in achieving the best outcome, as the integration of the pixel signal intensity map into the navigation system actually made the difference. This finding indicates that a holistic "anatomic and electroanatomic" approach is the key because it allows a complete identification of the arrhythmogenic substrate, an improved selection of the ventricular area to focus mapping, and finally better localization of the target ablation site (i.e., the conducting channel entrances).

CARDIOVASCULAR IMAGING IN CRT

Although CRT has been used for more than 2 decades, the proportion of patients who do not respond has remained nearly static (30% to 50%) over a period of extensive technological and technical development (27). Suboptimal response to CRT is multifactorial and may include suboptimal lead placement, ineffective delivery of biventricular pacing, and inappropriate selection of atrioventricular and interventricular delay (28). Moreover, an increasing number of clinical studies has demonstrated the importance of avoiding areas of myocardial fibrosis and targeting regions of latest mechanical activation. TARGET (Targeted Left Ventricular Lead Placement to Guide Cardiac Resynchronization Therapy) and STARTER (Speckle Tracking Assisted Resynchronization Therapy for Electrode Region) were both randomized controlled studies evaluating the use of speckle-tracking echocardiography for pre-procedural targeting of

FIGURE 6 Methods to Discriminate Left Atrial Fibrosis in Magnetic Resonance Imaging With Late Gadolinium Enhancement: Thresholding Techniques

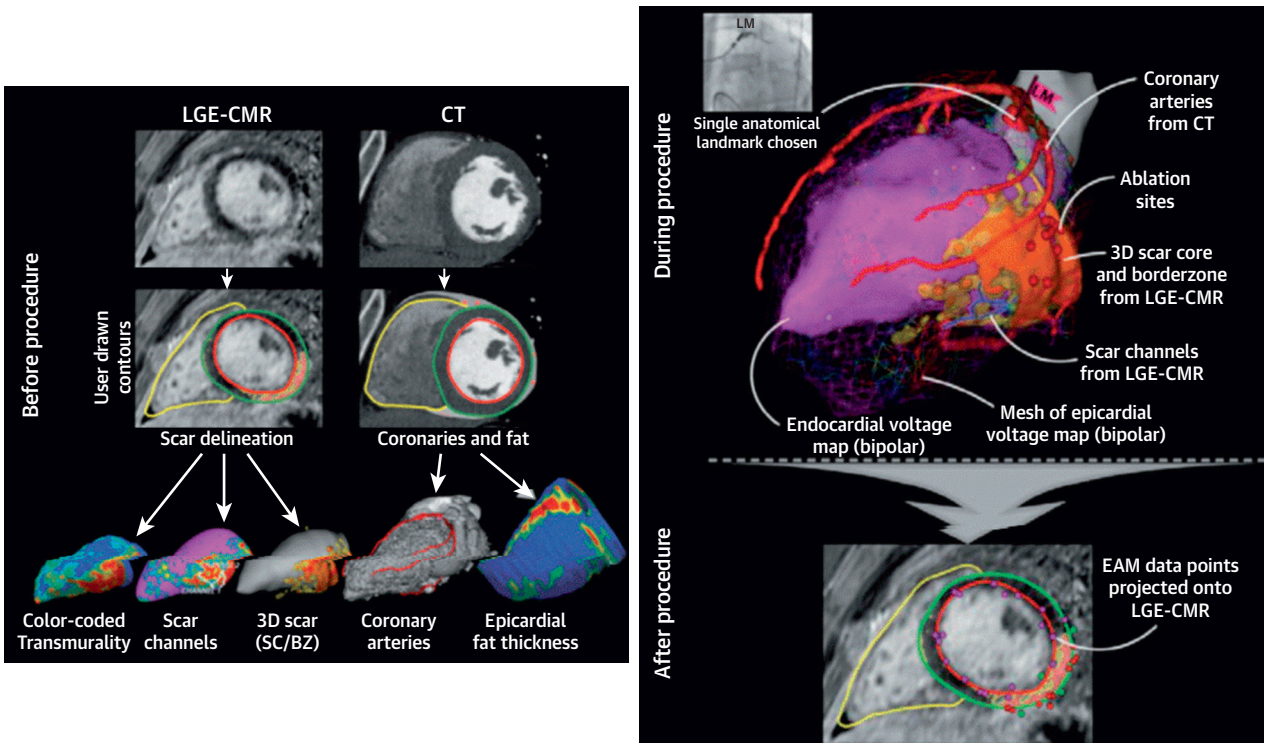


Bimodal distribution of pixel intensities of the left atrial (LA) wall. "Normal tissue" is defined as the first mode of lower pixel intensities and "injured tissue" at n SD above the mean pixel intensity of normal tissue, and histogram of pixel intensities: "normal" tissue is defined as the lower region of the pixel intensity histogram, between 2% and 40% of the maximum intensity within the LA wall. The fibrotic threshold was then calculated as 2 to 4 SDs above the mean of "normal" tissue. Comparative analysis of pre-existing fibrosis assessment methods in a healthy subject. The magnetic resonance image was processed with the addition of 2, 3, or 4 SDs above the mean of the normal myocardium (14) and also with the image intensity ratio (IIR) techniques using the validated cutoffs (0.97 to 1.61). Modified with permission from Pontecorboli et al. (20).

myocardial segments for LV lead delivery, compared with conventional non-image-guided implantation (29,30). Consistently, both studies showed that patients in which LV leads were placed in a region of latest mechanical activation had significantly reduced rates of HF hospitalization and death compared with those who had leads were placed otherwise. A large retrospective registry of 559 patients who had preprocedural CMR was performed demonstrated that patients with LV leads implanted in areas of myocardial fibrosis had a greater hazard ratio for cardiovascular death or HF hospitalization compared with those who had the leads were out of scar (31).

More recently, a selection of multimodality imaging studies has shown the additional benefit for avoiding scar and targeting dyssynchrony among patients being treated with CRT (32,33). A common theme among these studies is the observed improvement in CRT response rate (approximately 15% to 20%) in patients implanted using image-guided approaches. Although the results from the growing number of image guidance studies are encouraging, 1 of the major limitations is that the data output in each study is analyzed separately from radiography, rather than being integrated together. The variability in the rotation of the left- and right-sided chambers relative to each other, however, hinders the determination of regional anatomy with regard to lead position. Behar et al. (34,35) have recently published the first clinical study to evaluate a platform that enables the real-time analysis and fusion of CMR-derived scar and dyssynchrony data to guide LV lead implantation. Upon completion of a routine CMR scan, the patient is transferred to the adjacent catheter laboratory while the imaging dataset is processed within 25 min. Segmentation of long- and short-axis CMR sequences generates a 3D mesh along with a detailed location, burden, and transmurality of myocardial fibrosis. This process allows the identification of regions with the greatest dyssynchrony (**Figure 8**). Following a short registration step of the 3D model to the radiographic coordinate system, any subsequent radiographic acquisition is displayed with instantaneous overlay of the correctly oriented 3D model. Upon coronary venography, the 3D-derived model of the patient's left ventricle is instantaneously fused, thus enabling identification of the patient-specific target locations for LV lead placement and how they are subtended by the coronary venous tree (**Figure 8**). This platform was safely tested in 14 patients with conventional indications for CRT. It demonstrated that pacing with CMR-derived segments out of scar had more favorable electric properties and lower paced QRS duration than pacing

FIGURE 7 Example of Multimodal Image Integration to Facilitate Treatment Strategies



Pre-procedural late gadolinium enhancement (LGE) on cardiac magnetic resonance (CMR) shows scar channels (SCs) and border zone (BZ), whereas computed tomography (CT) shows coronary arteries and epicardial fat thickness. Both images are integrated in a mapping system in which normal voltage areas are depicted in **purple** for catheter ablation (scar dechanneling). Modified with permission from Sramko et al. (25). 3D = 3-dimensional; EAM = electroanatomic mapping.

FIGURE 8 Target Delivery of Cardiac Resynchronization Therapy

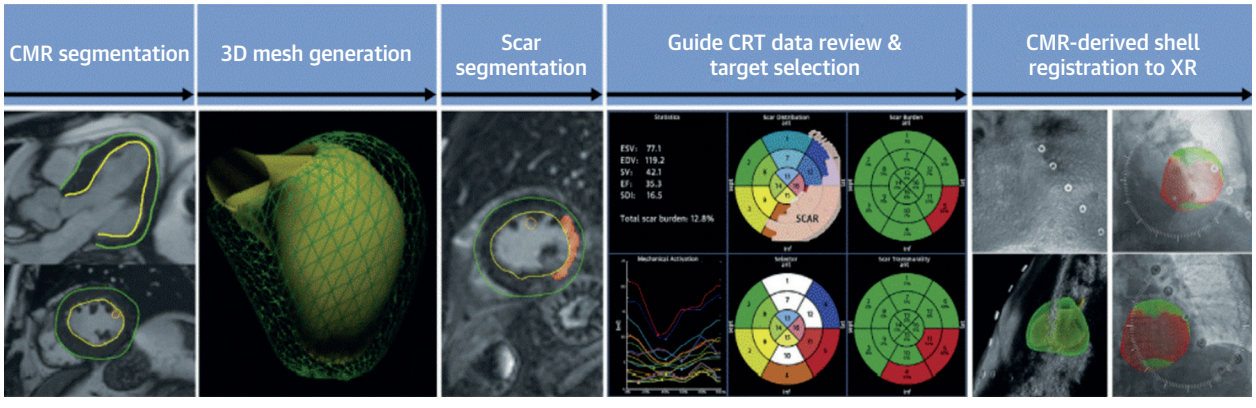
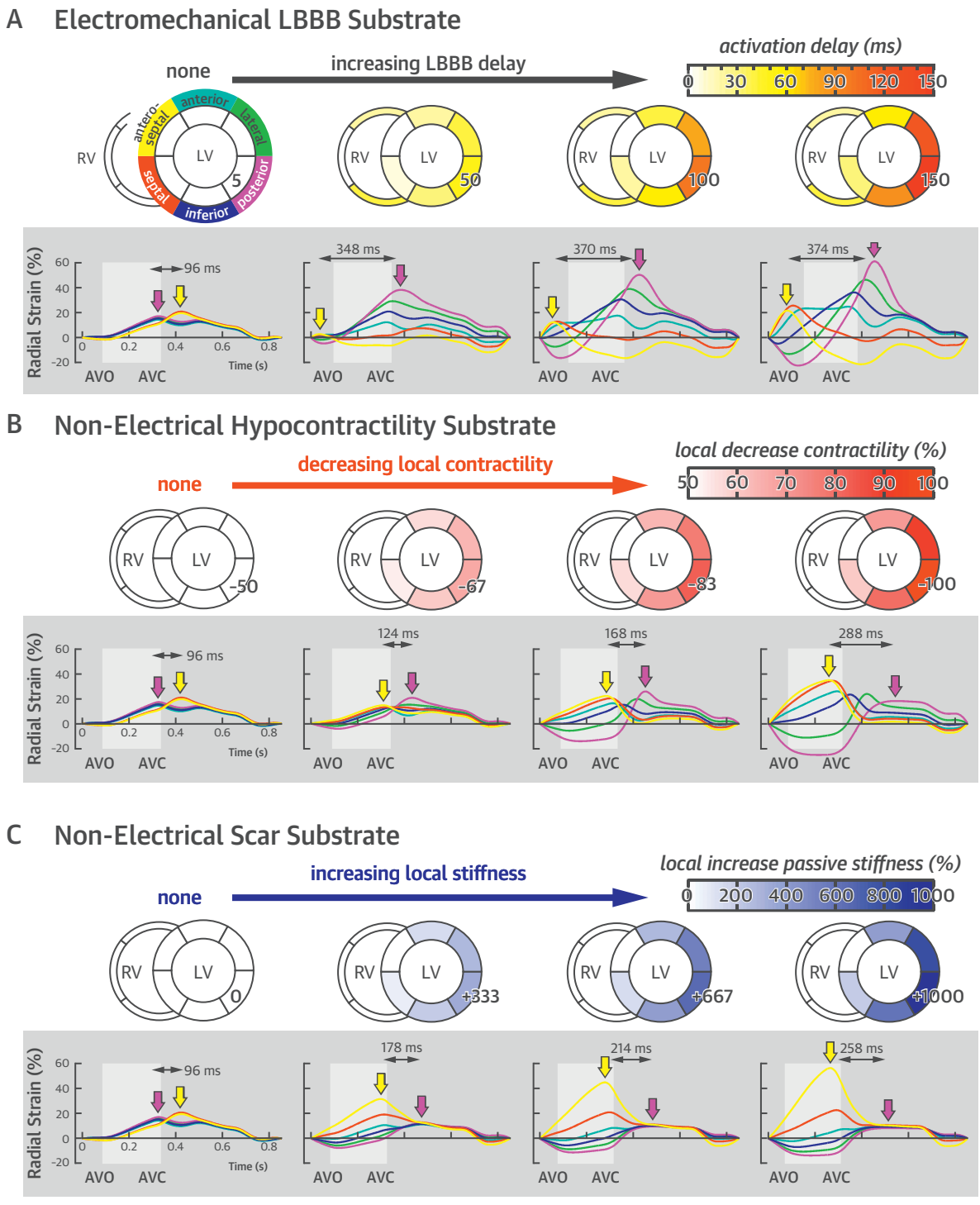


Image panel of workflow for real-time cardiac magnetic resonance–guided left ventricular lead implantation for targeted delivery of cardiac resynchronization therapy (CRT). Reproduced with permission from Behar et al. (34). 3D = 3-dimensional; CMR = cardiac magnetic resonance.

FIGURE 9 **Simulated Substrates of Mechanical Discoordination, Created by the CircAdapt Model**



Different myocardial substrates and corresponding regional strain developments in electric hypocontractile substrate or in a nonelectric hypocontractile substrate were simulated. Reproduced with permission from Lumens et al. (39). AVC = aortic valve closure; AVO = aortic valve opening; LBBB = left bundle branch block; LV = left ventricle; RV = right ventricle.

within CMR-derived regions of scar. Also, computed tomography may be used to systematically evaluate LV dyssynchrony, myocardial scar, and coronary venous anatomy in patients undergoing CRT, as recently shown by Truong et al. (36). These investigators demonstrated that computed tomographic wall motion dyssynchrony metrics and regional mechanical contraction analysis with LV lead location concordant to regions of maximal wall thickness were associated with 2-year major adverse cardiac events but not 6-month CRT response. Of course, 1 of the major drawbacks of computed tomography-based evaluation is the significant radiation exposure. Indeed, the effective radiation dose for the retrospective computed tomographic scan was 11.7 ± 5.0 mSv and the total radiation dose for delayed imaging was 13.5 ± 5.0 mSv. Using the patient's coronary venous anatomy, scar distribution electrophysiology, and mechanical contraction pattern to identify and target the optimal site for the LV lead is a novel approach to improving CRT effectiveness, thus representing personalized CRT for the 21st century. Larger scale, multicenter, randomized clinical trials will be required to demonstrate whether this approach yields greater CRT response compared with the conventional implantation method. Notably, despite the best-in-class imaging and lead technology for guiding quadripolar LV lead implantation in a single procedure (31–35), in about one-third of patients, a CMR-defined target segment, based on avoiding scar and targeting mechanical dyssynchrony, could not be achieved. This was because of the lack of coronary venous anatomy, resulting in placing the quadripolar LV lead adjacent to or in the scar. This observation strongly suggests that expecting responses >70% with a conventional transvenous CRT system in patients presenting mostly with ischemic etiology represents a utopic goal. As a consequence, an alternative treatment strategy is urgently needed; whether this solution would be an LV percutaneous epicardial approach or LV endocardial pacing remains to be determined. The recent emergence of LV endocardial stimulation as an alternative route for the delivery of biventricular pacing for CRT has growing evidence based on some data showing superior hemodynamic and electrophysiological indexes (35–37). The use of novel strategies that combine electric and mechanical (strain) assessment may be particularly suitable for an endocardial pacing approach, with the ability to target any region on the LV endocardial wall without the constraint of the coronary venous anatomy (38). The recent development of a wireless intracardiac LV endocardial electrode for CRT delivery represents a unique opportunity to use integrated multimodality image guidance for optimal LV site selection (35). Finally, recent developments in computer models of the dyssynchronous heart open new avenues in assisting physicians to better characterize myocardial substrate and in qualifying it as amenable to pacing response as well as to predict the response to pacing (28,39). A good example of clinically usable computer model-improved insight in disease mechanism and diagnosis is that of understanding of septal wall motion abnormalities, known as septal flash and septal rebound stretch, in patients with HF referred to CRT (**Figure 9**). The ultimate goal for the application of modeling for CRT would be to develop a full model of the heart of an individual patient in a way that does not disturb clinical workflow, to plan the best position for the pacing leads, and to test the effect of CRT ahead of implantation of the device.

HIGHLIGHTS

- Recent technological advances in cardiac imaging allow visualization of anatomic details up to millimeter size in 3D format.
- Electrophysiologists increasingly rely upon cardiac imaging for diagnosis, treatment, and management of patients with various arrhythmic disorders.
- Integration of diagnostic and interventional cardiac imaging will further increase the effectiveness of cardiac electrophysiological procedures.
- More extensive use of cardiac imaging will help in delivering patient-specific therapies with ablation and cardiac implantable electronic devices.

CONCLUSIONS

It is clear that device indication, implantation, and subsequent management have immensely benefited from the advances in cardiac imaging. In a similar way, electrophysiology has made significant progress in selecting those patients who may receive the greatest benefit from cardiac ablation, further improving the risk/benefit ratio, and more effectively using health care resources. Undoubtedly, the future integration of diagnostic and interventional cardiac

imaging will serve the ultimate goal of increasing effectiveness and efficiency of electrophysiological procedures and interventions as well as to deliver patient-specific therapies in cardiac electrophysiology and device indication and implantation.

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APPENDIX For supplemental videos, please see the online version of this paper.

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